

Remarks

Claims 21-40 are pending in the subject application. By this Amendment, Applicants have amended claims 21, 26, and 29. Support for the amendments can be found on page 17, lines 16-25; page 28, line 14; page 31, lines 3-10; and page 33, lines 15-25 of the subject specification, amongst other places. Entry and consideration of the amendments presented herein is respectfully requested. Upon entry of the above amendments, claims 21-40 will be before the Examiner.

Claims 21-40 are rejected under 35 U.S.C. §112, first paragraph, for lack of written description in the specification. Claims 21, 26, and 29 have been amended to delete reference to a "non-cross-linked" organic-inorganic composite. Accordingly, this aspect of the rejection has been rendered moot, and Applicants respectfully request withdrawal and reconsideration of the rejection under 35 U.S.C. §112, first paragraph.

Claims 21-40 are rejected under 35 U.S.C. §103 as obvious over Hayes *et al.* (1997) in view of Ogden *et al.* (1986) and Sumpter *et al.* (1990), and optionally Hayes *et al.* (1996) and Wang *et al.* (1996). Applicants respectfully traverse this ground of rejection because the combination of references fails to teach or suggest the invention as presently claimed. The combination of references does not provide the requisite expectation of success that the stationary phase could adhere to the inner surface of a column without a free radical cross-linking reaction. For example, they teach away from open tubular columns whose stationary phases are immobilized through means other than cross-linking reactions. Additionally, the combination of references fails to teach a coating bonded to the tube surface via an oxygen element.

Hayes 1997, which is co-authored by one of the inventors of the claimed invention, pertains to a capillary electrophoresis column whose coating was immobilized via cross-linking. More importantly, Hayes 1997 teaches that "[t]he cross-linking step was meant to provide higher operational stability to the polymeric coating." (Hayes *et al.* 1997 at 7) (emphasis added). Scheme 4 illustrates the cross-linking reaction recommended by Hayes 1997. (Hayes *et al.* 1997 at 7). This scheme shows cross-linking of the organic moieties attached to the silanol groups. Hayes 1997 fails to suggest additional coating structures that are immobilized without the step of cross-linking. Accordingly, the teachings of Hayes 1997 promote column stability by a cross-linking reaction.

The remaining references fail to remedy this deficiency of Hayes 1997. Sumpter *et al.* suggest that small internal diameter open tubular columns (*e.g.*, capillaries) are "impractical, unless a

highly viscous stationary phase is coated and immobilized (cross-linked) in a short period of time.” (Sumpter *et al.* at p 508). Moreover, the type of cross-linking utilized by Sumpter *et al.* is a cross-linking reaction initiated by an azo-*tert*-butane-argon purge, which is specifically excluded by the columns of the present invention. Sumpter *et al.* also provide a synopsis of difficulties associated with coating capillary coatings. It explains how Raleigh instability results in both stationary phase rearrangement and loss of efficiency and suggests that immobilization via cross-linking successfully addresses the issues raised by Raleigh instability. Accordingly, the teachings of Sumpter *et al.* in combination with Hayes 1997 would lead a skilled artisan to expect that the stationary phases of the capillaries of the present invention would rearrange so quickly that a subsequent chromatographic separation could not take place.

Similarly, the addition of Ogden *et al.* fails to remedy this deficiency of the combination of Sumpter *et al.* and Hayes 1997. Ogden *et al.* also suggest that improved stationary phase stability is obtained when cross-linking occurs. (Ogden *et al.* at 7). As in Sumpter *et al.*, the cross-linking of Ogden *et al.* is derived from a cross-linking reaction (*i.e.*, cross-linking via reaction with azo-*tert*-butane). Moreover, they teach that column performance can be “dramatically improved” by immobilizing the column’s stationary phase. (Ogden *et al.* at 7). Ogden *et al.* fails to provide any other suggestion that the stationary phase is stable in the absence of a cross-linking immobilization.

The optional references, Hayes 1996 and Wang 1996, also fail to remedy the aforementioned deficiencies. Hayes 1996, which is co-authored by the inventors of the present invention, relates to capillary electrophoresis (CE) columns. Hayes 1996 also suggests a coating immobilized with cross-linking reactions initiated by a strong radical (*i.e.*, dicumyl peroxide). Similarly, the columns of Wang 1996, which is authored by the present inventors, are also immobilized with cross-linking. (Wang *et al.* 1996 at 507). Neither Hayes 1996 nor Wang 1996 suggest immobilization of their respective coatings by any means other than cross-linking reactions.

Surprisingly, the capillaries of the claimed invention are not only stabilized without the use of a cross-linking reaction, the capillaries produce superior separations than what was previously known. As discussed on page 5 of the Declaration under 37 C.F.R. 1.132 dated June 9, 2005, which is hereby incorporated by reference, the columns of the claimed invention exhibit “highly efficient separations represented by narrow peaks” that are demonstrated in Figures 7-39 of the instant application. (06/09/05 Declaration under 37 C.F.R. 1.132 at 5). In other words, the stationary phases

of the claimed columns did not destabilize or suffer from Rayleigh's instability as suggested by the cited references; instead, the columns successfully separated a wide variety of components including aldehydes, ketones, fatty acids, *etc.* Specifically, the claimed columns' performance, in comparison to similar separations discussed in Wang 1996 and Ogden *et al.*, is quite efficient and stable in spite of their immobilization without cross-linking. Not only did the claimed columns efficiently separate their target analytes, they did so without undergoing the instabilities expected by each of the other references.

For example, a Grob mixture was chromatographically separated by both the claimed columns, as demonstrated in Figures 20-22, and the Ogden *et al.* column (Ogden's Figure 5). Surprisingly, in view of the teachings of the cited references, the peaks of the claimed columns' chromatograms are narrow and exhibit excellent baseline stability. This indicates an efficient, success separation using a stable gas chromatographic column. Similar efficient separations of dimethylphenol isomers are observed in the claimed columns (Figure 9) in comparison to Wang 1996's columns (Figure 3) and of *cis*- and *trans*-stilbene by the claimed columns (Figure 29) versus Wang 1996 (Figure 4). The claimed columns consistently separated the mixtures as shown by the narrow peaks of the chromatograms. Although the teachings of Hayes 1997, Sumpter *et al.*, Hayes 1996, and Wang 1996 all suggest the instability of separation columns whose coatings are not immobilized by cross-linking, the current invention consistently and surprisingly separates a wide variety of its target analytes including, for example, aromatics, amines, anilines, glycols, isomers of alcohols, ketones, fatty acids, halogenated carboxylic acids, aldehydes, and C₁₂-C₃₁ FAMES, amongst many other target analytes. Accordingly, the combination of references fails to render the claimed columns non-obvious because the claimed columns were not rendered unstable as suggested by the cited art.

Moreover, the combination of references fails to teach a stationary phase coating that is deactivated in three dimensions (*i.e.*, at both the column's inner surface and within the stationary phase coating). These references discuss the deactivation of a surface but fail to teach the deactivation through a stationary phase coating. For example, Hayes 1997 only discusses deactivating the surface silanol groups. (Hayes *et al.* at 6). Its deactivation steps focus on modifying the silanol groups at the surface of Hayes 1997 columns. None of the schemes illustrate any deactivation of silanol groups in the coating itself. For example, scheme 4 clearly shows -Si-OH

J:\USF\221XT\PTO\response.2.doc/DNR/umh

10

Docket No. USF-221XT
Serial No. 09/763,419

groups throughout the coating. Without deactivation, these groups will likely undergo absorptive interactions and reduce column efficiency. Moreover, both Odgen *et al.* and Sumpter *et al.* focus on deactivation at the inner surface of a column. In fact, each of these columns' inner surfaces are deactivated before the coating solution contacts the capillary's inner surface. Thus, the coating is not deactivated within the coating of either Ogden *et al.* or Sumpter *et al.* The optional references fail to remedy this deficiency and do not suggest deactivation within the coating.

Additionally, Hayes 1997 fails to teach or suggest a sol-gel coating chemically bonded to the inner tube surface through an oxygen element. Hayes 1997 illustrates its coating throughout the paper and specifically, in schemes 2, 3, and 4, shows that its cross-linked coating is attached to its column inner surface via a -Si- element. (Hayes *et al.* at 7-9). It does not suggest alternative bonding schemes other than through the -Si- element. The remaining secondary references fail to remedy this deficiency. They provide no actual teachings or suggestions on the specific bonding sites that adhere their respective sol-gel coatings to the columns' inner surfaces. Accordingly, Applicants respectfully request the reconsideration and withdrawal of the rejection under 35 USC §103(a).

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



Jenna M. Morrison

Patent Attorney

Registration No. 55,468

Phone No.: 352-375-8100

Fax No.: 352-372-5800

Address: P.O. Box 142950

Gainesville, FL 32614-2950

JMM/amb

JAUSF221X NPTO response.2 doc/DNB/amb